Supplementary materials

**Excluded following baseline and follow-up review (*n*=16):**

**Dementia (at baseline) (*n*=8)**

**Subjective impairment only (*n*=3)**

**Voluntarily withdrew prior to provision of study data (*n*=5)**

**≥ 2 Clinical Diagnostic Core Features:**

**Probable MCI-LB**

 ***n*= 44**

**No Clinical Diagnostic Core Features:**

**MCI-AD**

***n*=39**

**Consented to SUPERB study:**

***n*= 120**

**MCI:**

***n*=104**

**One Clinical Diagnostic Core Features:**

**Possible MCI-LB**

***n*=21**

**Appendix Figure A1. Flowchart showing the screening, consent and diagnostic group allocation of participants with Mild Cognitive Impairment.**

**Appendix Table A1. Cognitive outcome measures by group for MCI with Lewy bodies (MCI-LB; *n*=44) and MCI due to Alzheimer’s disease (MCI-AD; *n*= 39), with significance (*p*) and Wilcoxon rank-sum (*r*) or Cohen’s *d* effect sizes for between-group comparisons of MCI subtypes.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **MCI-AD** | **MCI-LB** | ***p*** | **Effect size** |
| MMSE, mean (SD) | 26.9 (2.1) | 26.4 (2.5) | 0.38 | *d=*0.22 |
| *Verbal* |  |  |  |  |
| GNT, mean (SD) | 19.2 (4.9) | 20.6 (4.7) | 0.19 | *d=*0.29 |
| RAVLT Maximum T1:T5, mean (SD) | 8.4 (2.9) | 8.2 (2.5) | 0.70 | *r=*0.02 |
| RAVLT Learning, median (IQR) | 3.6 (2.8) | 4.0 (2.7) | 0.56 | *r=* 0.08 |
| RAVLT Short Delay, median (IQR) | 3.0 (1.0-3.0) | 5.0 (3.0-7.0) | 0.16 | *r=*0.17 |
| **RAVLT Long Delay, median (IQR)** | **1.0 (0.0-6.3)** | **5.0 (2.0-8.0)** | **0.04** | ***r=*0.23** |
| **RAVLT % Max Recalled, median (IQR)** | **15.5 (0.0-70.7)** | **58.6 (27.7-80.8)** | **0.01** | ***r=*0.28** |
| *Visuospatial* |  |  |  |  |
| Corsi Blocks (span), median (IQR) | 5.0 (3.5-5.0) | 4.0 (3.0-5.0) | 0.51 | *r=*0.08 |
| MTCF copy, median (IQR) | 32.8 (30.0-35.0) | 32.0 (28.0-35.0) | 0.81 | *r=*0.03 |
| MTCF recall, median (IQR) | 8.25 (5.0-12.0) | 10.5 (7.0-14.0) | 0.06 | *r=*0.23 |
| **MTCF %recall, mean (SD)** | **0.27 (0.16)** | **0.37 (0.15)** | **0.01** | ***d*=0.65** |
| VPT, median (IQR) | 17.4 (12.0-18.0) | 17.2 (10.0-18.0) | 0.49 | *r=*0.09 |
| *Executive Function* |  |  |  |  |
| FAS, mean (SD) | 36.0 (11.7) | 31.9 (13.6) | 0.20 | *d*=0.32 |
| Stroop CW, median (IQR) | 21.0 (7.5-26.0) | 19.5 (13.0-28.8) | 0.33 | *r=*0.12 |
| **Trails B, median (IQR)** | **100.8 (69.5-172.0)** | **115.9 (90.0-214.0)** | **0.03** | ***r=*0.26** |
| **Trails Ratio (A/B), mean (SD)** | **838.1 (0.7)** | **837.7 (0.8)** | **0.04** | ***d=*0.52** |
| Digit Span Backwards, median (IQR) | 5.0 (4.0-7.0) | 5.0 (4.0-6.0) | 0.96 | *r=*0.01 |
| *Processing Speed* |  |  |  |  |
| Digit Span Forward, median (IQR) | 8.0 (6.0-10.0) | 9.0 (7.0-10.0) | 0.28 | *r=*0.12 |
| Trails A, median (IQR) | 44.9 (36.0-65.0) | 47.9 (38.4-74.8) | 0.39 | *r=*0.10 |
| **DSST, mean (SD)** | **31.5 (12.6)** | **26.3 (9.0)** | **0.04** | ***d=*0.48** |
| Symbol Copy, median (IQR) | 75.0 (56.0-89.0) | 65.0 (48.0-88.0) | 0.11 | *r=*0.18 |
| **Error Check, median (IQR)** | **41.0 (33.0-46.0)** | **31.0 (20.0-37.0)** | **<.001** | ***r=*0.36** |
| **Stroop W, median (IQR)** | **78.0 (66.3-87.8)** | **63.5 (50.3-78.8)** | **0.01** | ***r=*0.29** |
| SRT mu correct, median (IQR) | 282.4 (248.8-340.5) | 279.4 (245.7-353.4) | 0.89 | *r=*0.02 |

**Appendix Table A2. 5th and 16th percentile standings of MCI-Probable and MCI-AD patients relative to control data (% of group) on neuropsychological outcome measures.**

|  |  |  |
| --- | --- | --- |
|  | **MCI-LB Probable** | **MCI-AD** |
|  | **5th** | **16th** | **5th** | **16th** |
| MMSE | 45.5 | 54.5 | 38.5 | 48.7 |
| *Verbal* |  |  |  |  |
| GNT | 9.1 | 43.2 | 21.9 | 59.0 |
| RAVLT Maximum | 38.6 | 45.5 | 43.6 | 48.7 |
| RAVLT Learning | 13.6 | 50.0 | 18.2 | 57.7 |
| RAVLT Short Delay | 38.6 | 54.5 | 59.0 | 69.2 |
| RAVLT Long Delayed Recall | 27.3 | 43.2 | 59.0 | 66.7 |
| RAVLT % Maximum recalled | 25.0 | 36.4 | 25.6 | 64.1 |
| *Visuospatial* |  |  |  |  |
| Corsi Blocks | 29.5 | 52.3 | 25.6 | 48.7 |
| MTCF copy | 40.9 | 59.1 | 48.7 | 60.3 |
| MTCF recall | 29.5 | 53.4 | 43.6 | 71.8 |
| MTCF % recall | 15.9 | 45.5 | 41.0 | 69.2 |
| VPT | 58.8 | 64.7 | 53.8 | 61.5 |
| *Executive Function* |  |  |  |  |
| FAS | 40.9 | 43.2 | 30.8 | 42.3 |
| Stroop CW | 50.0 | 72.7 | 41.0 | 79.5 |
| Stroop Ratio Interference | 29.5 | 47.7 | 41.0 | 71.8 |
| Trails Ratio (A/B) | 4.5 | 4.5 | 0 | 7.7 |
| Digit Span Backwards | 0.0 | 26.1 | 7.7 | 28.2 |
| Trails B | 54.5 | 84.1 | 38.5 | 64.1 |
| *Processing Speed* |  |  |  |  |
| Digit Span Forward | 2.3 | 12.5 | 2.6 | 23.1 |
| Trails A | 38.6 | 68.2 | 35.9 | 59.0 |
| DSST | 43.2 | 88.6 | 20.5 | 64.1 |
| Symbol Copy | 47.7 | 70.5 | 28.2 | 61.5 |
| Error Check | 45.5 | 61.4 | 17.9 | 33.3 |
| Stroop W | 38.6 | 56.8 | 15.4 | 41.0 |
| Simple Reaction Time | 15.9 | 56.8 | 12.8 | 38.5 |

**Appendix B. PCA and composite calculation**

In addition to univariate analyses of task outcome measures, data-driven composite scores were created following principal components analysis (PCA) for use in hierarchical linear modelling (HLR) was used following data-reduction techniques in order to (1) act as a data reduction technique prior to multivariate analyses and (2) more fully capture the breadth of broader cognitive domains (e.g. verbal memory) than if using single outcome measures. PCA was used as a data-reduction technique prior to multivariate analysis following the recommendations of Field (2009) and Stevens (2002). Of tests with multiple possible outcome measures, the most representative of specific cognitive processes were entered. Approximately one-quarter of VPT scores were missing due to time constraints of testing and were therefore excluded. Remaining variables had a maximum of *n*=19 (16.2%) missing data points. Little’s Missing Completely at Random Test (MCAR) on variables except those derived from others (RAVLT %Maximum recalled, for e.g.) was not significant, χ2(451) = 480.3, *p* = .164. SPSS’s expectation-maximization approach was used to replace the missing values from 19 variables and the derived values were then re-computed. As standard exclusion of low-loadings (r<.03) may be too lenient a criterion for PCA data cleaning, correlation matrices were inspected before entry into the PCA for any extreme values or extremely high, weak or nonsignificant correlations between variables (see supplementary materials; Stevens, 2002). A formula based on the sample size and a more stringent alpha level of .01 was used to evaluate loadings in the PCA solutions to avoid errors due to multiple comparisons (absolute value of 0.722; Hair, Anderson, Tatham, & Black, 1998; Stevens, 2002). Composites scores based on the PCA results were computed as average *z*-scores and retained single outcome measures were converted to control-adjusted *z*-scores.

In controls, the iterative process of adding and removing variables until convergence between Structure and Pattern matrices was achieved using Oblimin rotation and 77.2% cumulative variance explained (KMO =.732) by three components. The first component (48.0%), loaded onto psychomotor variables (Trails A, Symbol Copy), some with cognitive/executive weighting (Stroop CW, Error Check). Component 2 (16.6%) represented verbal learning (RAVLT Max and Short Delay recall) and Component 3 was only loaded by MTCF Recall and Graded Naming, explaining 12.6% variance. Re-run using MCI-LB data, the final model explained 80.5% cumulative variance with four components (KMO = .725). Component 1 can be interpreted as visuospatial working memory (Corsi, VPT; 37.3% of variance), Component 2 as verbal learning and memory (RAVLT Max and Short delay; 19.6%), Component 3 as executive function, cognitive and psychomotor speed (FAS, DSST, Symbol Copy; 13.5%), and Component 4 as visuoconstruction and verbal naming (MTCF Copy, Graded Naming; 10.1%). Finally, using MCI-AD data only, the process resulted in an unstable three-factor solution that explained a total variance of 72.6% (KMO=.709). Throughout the process, verbal and visuospatial memory measures (MTCF %Recall, RAVLT Max, Short and Long Delay) loaded together consistently (Component 1), with executive, psychomotor and processing variables (FAS, Trails B, DSST, Symbol Copy, Stroop C, SRT) and visuospatial working memory (VPT) forming components 2 and 3, respectively.

Two composite scores were calculated based on the results of the exploratory PCA. Firstly, a “verbal learning and memory” composite (RAVLT Maximum and Short Delay) was created using the variables that loaded together consistently onto a single component in all groups. Secondly, a “visuospatial working memory” composite was calculated from Corsi and VPT, informed by the MCI subtypes results. Control data emphasized a “visuospatial delayed memory” component captured by MTCF %Recall. A theory-driven Executive Function composite consists of FAS and Trails Ratio. MCI-LB and MCI-AD did not differ significantly in Visuospatial Working Memory, *t*(81) = .741, *p*=.461, nor Verbal Learning and Memory, *U* = 778.5, *p*=.468, composite scores. MCI-AD scored significantly lower on Visuospatial Memory (IQR: -1.4 [-2.0,-0.9]) than MCI-LB (IQR: -1.1 [-1.7,-0.5]), *U* = 628.5, *p*=.036, *d*=0.5, and Verbal Memory (IQR: -2.2 [-2.5,-0.7]) than MCI-LB (IQR: -1.3 [-1.9,-0.1]), *U* = 605.5, *p*=.020, *d*=0.4.

References

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Stevens, J. P. (2002). *Applied multivariate statistics for the social sciences* (4 ed.). Mahwah, New Jersey: Lawrence Erlbaum Associates.